

INSTITUTIONAL ETHICS COMMITTEE



Nizam's Institute of Medical Sciences
PUNJAGUTTA, HYDERABAD, INDIA



Protecting Participants
Guiding Researchers



STRUCTURE OF INSTITUTIONAL ETHICS COMMITTEE

- * Establishing and Constituting Authority - Director
- * Chairperson - Dean
- * Member Secretary - Head, Department of Clinical Pharmacology and Therapeutics
- * Members of IEC
 - 2 Medical Scientists
 - 2 Non-Medical Scientists
 - 1 Lay person
 - 1 Legal expert or judge

IEC WORKING MANUAL

This document

for

Institutional Ethics Committee

of

Nizam's Institute of Medical Sciences

is

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Procedure for Establishing and constituting IEC:

Director (Head of the institute) will establish and constitute an Ethics committee to ensure a competent review of all ethical aspects of the project proposals received and execute the same free from any bias and influence that could affect their objective.

Head of Institute will consider the institutional interest before any project is forwarded for the EC review.

1. IEC will be multidisciplinary and multisectorial in composition including relevant scientific expertise, balanced age, and gender distribution and a lay person.
2. IEC will be established in accordance with the applicable laws and regulations of the state, country and in accordance with the value and principles of the communities they serve.

Responsibilities of the IEC:

1. To protect and safeguard the dignity, rights, safety and well being of all actual or potential research participants.
2. To consider the principle of justice, that the benefits and burdens of research be distributed fairly among all groups and classes in society taking into account age, gender, economic status, culture and ethic consideration.
3. To provide advise to the researchers on all aspects of the welfare and safety of research participants after ensuring the scientific soundness of the proposed research.

Composition:

IEC will have a chairman and the member secretary nominated by the Director.

IEC will have total eight (8) members including

- 2 medical scientists ,
- 2 non medical scientists,
- 1 nonscientist (lay person,)
- 1 legal expert or retired judge.

Procedure for Membership appointment:

Director will nominate the members of IEC, who have the qualification and experience to review and evaluate the science, medical aspect and ethics of the proposed study. Conflict of interest will be avoided when making appointments, but where unavoidable there will be transparency with regards to such interest.

When needed IEC will invite subject experts, if required to offer their views

1. The normal term for IEC member will be for 24 months.
 2. Director can renew the appointment of the member on the basis of contribution.
 3. During the term, Director can disqualify any member if the contribution is not adequate and or there is long period of (member) non availability
 4. Member can discontinue from membership of IEC after giving at least 1month advance notice.
 5. Director can replace the member of IEC as and when required
 6. Each member is required to sign the declaration and confidentiality agreement regarding IEC activities.
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Quorum requirements:

1. Minimum 5 members are required to compose the quorum
2. No quorum should consist entirely of members of one profession. Quorum will include at least one member as non scientific (lay person), at least one who is independent of the Nizam's Institute of Medical Sciences and at least one medical scientist.

Review procedure:

1. IEC will review every research proposal on human subject.
2. Every proposal will be evaluated by a scientific review committee, to ensure the scientific soundness and technical excellence of the proposed research, before it is taken up for main IEC review.

The IEC will evaluate the possible risks to the subject with proper justifications, the expected benefit and adequacy of documentation for ensuring privacy, confidentiality and justice issue.

The IEC review will be done through formal meetings and will not restore to decision through circulation of proposal.

Meeting requirements:

- All the IEC meeting will be held regularly as scheduled dates that are announced and notified in advance. Additional review meetings can also be held with short notice as and when required.
- Meetings will be planned in accordance with the need of the work load.
- Member will be given 10 days time in advance to review study proposals and the relevant documents.
- IEC meetings will be minuted and all the proceedings and deliberation will be documented
- Signatures of all the members who have participated in the meeting will be obtained.
- At the end of each IEC meeting, signatures from each member who has participated will be obtained on the final draft of the minutes of meeting
- Applicant, sponsor or investigator may be invited to present the proposal or elaborate on specific issues.
- Independent expert may be invited to the meeting or to provide written comment, subject to applicable confidentiality agreement.

Procedure for communicating the decision of IEC to the applicant:

- A decision of the IEC will be communicated to the applicant in writing, within two weeks of the meeting at which the decision was taken. The communication of the decision will include:
 - Name and address of IEC.
 - The date and place of decision
 - The name and title of the applicant.
 - Title of the research proposal reviewed.
 - The clear identification of protocol no, version number date and or amendment no, date
 - Names and number of all documents reviewed, including, applicant's CV, subject information sheet, informed consents etc.
 - A clear statement of decision reached
 - Any advice by the IEC to the applicant.

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- In case of conditional decision any requirement by IEC, including suggestions for revision, and the procedure for having the application re-reviewed.
 - List of members participated, with their decision in favor /or against the proposal
 - List of member who did not participate.
 - In case of negative decision, clearly stated reasons for the negative decision will be given.
 - Signature (dated) of the chairman (or his authorized person of the IEC).

Procedure for decision making:

In making decision on application for the ethical review of any research proposal, IEC will consider the following:

- Member having the conflict of interest will indicate to the chairman prior to the review of application and same will be recorded in the minutes.
- Where there is conflict of interest, member will withdraw from the decision making procedure.
- A decision will only be taken when sufficient time has been allowed for the review and discussion of an application and in absence of non members.
- Decision will only be taken at meetings where a quorum is complete.
- Decision will be taken only after reviewing a complete application with all the required documents necessary for proposal, consideration has been examined by IEC.
- Only members who participated in review and discussion will participate in decision.
- Wherever possible, the decision will be arrived through consensus not by vote, but when a consensus appears unlikely voting can be performed.
- Decision procedure will specify the conditional decision, with clear suggestions and re-review procedure.
- Negative decision will be supported by clearly stated reasons.

Procedure for Submission of application for ethical review :

1. The principal Investigator has to submit an application in a prescribed format (Form - I) along with study protocol for the review of the IEC.
2. Application can be submitted to the office of the Chairman, IEC, Nizam's Institute of Medical Sciences, Hyderabad on any working day.
3. All the proposals and documents must be submitted in English language, at least 3 weeks in advance from the schedule date of IEC meeting.
4. Eleven (11) copies of study proposal (with all documents and an undertaking in prescribed format Appendix I) must be submitted along with application form duly signed and dated by the investigator(s)
5. On receipt, the applications will be acknowledged including the completeness of an application by the IEC office.
6. Every application will be acknowledged with IEC registration number to be used for all future correspondence and references. (Form - II)

Procedure for expedited review:

IEC will receive and consider the proposal for the expedited approval for the studies having

1. No or minimum risk to the trial participants.
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2. Re examination of a proposal already examined by the IEC
 3. Study of minor nature eg. examination of case records
 4. An urgent proposal of national interest having minimum risk

All expedited approval will be given in a meeting with quorum of at least 3 members (nominated by the Chairman) of IEC are present. Quorum must have one expert or scientist having scientific knowledge in the field of proposal.

Decision taken by the committee on expedited approval however will be brought to the notice of the main committee members.

Follow up procedure.

- IEC will review and progress of all the studies for which a positive decision has been reached from the time of decision till the termination of the research.
- Progress of all the research proposals will be followed at a regular interval of at least once a year. But in a special situations, IEC will conduct the follow up review at shorter intervals basing on the need, nature and events of research project.
- All the requirements and procedures for follow up review will be similar to that of initial and main review.
- Following instances and events will require the follow-up review
 - i. Protocol amendment, likely to affect, rights safety, or well being of research subject of conduct of study.
 - ii. Serious or unexpected ADR related to study or product, action taken by investigator, sponsor and regulatory authority.
 - iii. Any event or information that may affect the benefit/risk ratio of the study.

A decision of a follow up review will be issued and communicated to applicant indicating modification / suspension/ termination/ continuation of the project.

In case of premature suspension/termination, the applicant must notify the IEC of the reasons for suspension/termination with a summary of results.

Applicant must inform at the time of completion of study and must send the result summary to IEC.

IEC must receive a copy of final summary of study completed from the applicant.

Procedure for documentation and archiving:

All the documents and communications of IEC will be dated, filed and archived in a secured place.

Only person ,who is authorized by the chairman of IEC will have the access for the various documents.

All the documents related to research proposals will be archived for a minimum period of 3 years in the institute, following the completion of the study.

No document (except agenda) will be retained by any IEC member.

At the end of each meeting every member will return all the research proposal documents to IEC office staff.

Following documents will be filed and archived with proper label on the top of file for easy identification of proposal.

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1. The constitution, written standard operating procedures of the EC, and regular (annual) reports.
 2. The curriculum vitae of all EC members
 3. A record of all incomes and expenses if any, of the EC, including allowances and reimbursements made to the secretariat and EC members;
 4. The published guidelines for submission established by the EC.
 5. The agenda of the EC meetings;
 6. The minutes of the EC meetings
 7. One copy of all materials submitted by an applicant;
 8. The correspondence by EC members with applicants or concerned parties regarding application, decision and follow-up;
 9. A copy of the decision and any advice or requirements sent to an applicant.
 10. All written documentation received during the follow-up;
 11. The notification of the completion, premature suspension, or premature termination of a study.
 12. The final summary or final report of the study.

Element of the Review:

Following are the element to be reviewed by the IEC member

Scientific design and conduct of the Study. (Appendix - III)

1. The appropriateness of the study design in relation to the objectives of the study, the statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants.
2. The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
3. The justification for the use of control arms;
4. Criteria for prematurely withdrawing research participants;
5. Criteria for suspending or terminating the research as a whole.
6. The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a data safety monitoring committee (DSMC).
7. The adequacy of the site, including the supporting staff, available facilities and emergency procedures;
8. The manner in which the results of the research will be reported and published..

Recruitment of research participants:

1. The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status and ethnicity).
 2. The means by which initial contact and recruitment is to be conducted.
 3. The means by which full information is to be conveyed to potential research participants or their representatives.
 4. Inclusion criteria for research participants
 5. Exclusion criteria for research participants.
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Care and protection of research participants:

1. The suitability of the investigator(s)'s qualifications and experience for the proposed study;
2. Any plans to withdraw or withhold standard therapies for the purpose of the research and the justification for such action;
3. The medical care to be provided to research participants during and after the course of the research;
4. The adequacy of medical supervision and psycho-social support for the research participants.
5. Steps to be taken if research participants voluntarily withdraw during the course of the research.
6. The criteria for extended access to the emergency use of and/or the compassionate use of study products;
7. The arrangements, if appropriate for informing the research participants general practitioner (family doctor), including procedures for seeking the participant's consent to do so.
8. A description of any plans to make the study product available to the research participants following the research;
9. A description of any financial costs to research participants.
10. The rewards and compensations for research participants (including money, services, and /or gifts).
11. The provisions for compensation/treatment in the case of the injury disability/ death of a research participant attributable to participation in the research.
12. The insurance and indemnity arrangements.

Protection of research participant confidentiality:

1. A description of the persons who will have access to personal data of the research participants, including medical records and biological samples;
2. The measures taken to ensure the confidentiality and security of personal information concerning research participants;

Informed consent process:

1. A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent;
2. The adequacy, completeness, and understandability of written and oral information to be given to the research participants and when appropriate, their legally acceptable representative(s).
3. Clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals;
4. Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation (including their rights, safety and well-being).
5. The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project;

Community considerations:

1. The impact and relevance of the research on the local community and on the concerned communities from which the research participants are drawn.
2. The steps taken to consult with the concerned communities during the course of designing the research;

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3. The influence of the community on the consent of individuals.
 4. Proposed community consultation during the course of the research
 5. The extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research and the ability to respond to public health needs;
 6. A description of the availability and affordability of any successful study product to the concerned communities following the research.
 7. The manner in which the results of the research will be made available to the research participants and the concerned communities.

Application for Ethical Review of Biomedical Research Proposal

To

The Chairman
Institutional Ethics Committee
Nizam's Institute of Medical Sciences
Hyderabad

Date:

Full name of applicant : _____

Designation:

Complete Postal Address:

Tel.No: (O) _____ (R) _____

(Fax)

e-mail:

Site of study:

Protocol No.

Version:

Date:

Amendment No.

Version:

Date:

Title of Project:

Sponsor Name:

Address:

Name

Signature:

Principal Investigator:

Co-investigator : 1.

2.

3.

Type of study : National / International

Type of Trial : Single center / multi center

Name & Signature of applicant

Date:

(Application must be submitted along with all essential documents for the review)
(See List of Documents - Appendix - I)

Institutional Ethics Committee
Nizam's Institute of Medical Sciences, Hyderabad
Acknowledgement

Date: _____

* Study Proposal Registration No. NIMS - IEC / 2002 / 0 _____

Received _____ copies of study proposal.

Protocol No. _____

Version: _____

Dated: _____

Amendment No.: _____

Version: _____

Dated: _____

Entitled _____

From Dr. _____

Designation _____

Address _____

For ethical review:

* Name of IEC Staff

* Signature:

receiving application:

* Date:

* For official use only. Not to be filled by the applicant.

(To filled by the applicant in duplicate)

Appendix - I

List of documents to be submitted along with application for the IEC Review

1. Signed and dated application form on prescribed format
 2. The protocol of the proposed research (clearly identified, numbered and dated), together with supporting documents and annexes;
 3. A summary (as far as possible in non-technical language, synopsis, or diagrammatic representation (flowchart) of the protocol;
 4. A description (usually included in the protocol) of the ethical considerations involved in the research;
 5. Case report forms diary cards and other questionnaires intended for research participants.
 6. In case the research involves a study product (such as a pharmaceutical or device under investigation, an adequate summary of all safety, pharmacological pharmaceutical and toxicological data available on the study product, together with a summary of clinical experience with the study product to date (e.g.: recent investigator's brochure published data, a summary of the product's characteristics); (Product information)
 7. Investigator(s) curriculum vitae (updated, signed and dated)
 8. Material to be used (including advertisements) for the recruitment of potential research participants;
 9. A description of the process to be used to obtain and document consent;
 10. Written and other forms of information for potential research participants (clearly identified and dated) in the language(s) understood by the potential research participants and, when required, in other languages;
 11. Informed consent form (clearly identified and dated) in the language(s) understood by the potential research participants and when required in other languages.
 12. A statement describing any compensation for study participation (including expenses and access to medical care) to be given to research participants;
 13. A description of the arrangements for indemnity, if applicable;
 14. A description of the arrangements for insurance coverage for research participants, if applicable
 15. A statement of agreement to comply with ethical principles set out in relevant guidelines as an undertaking (Appendix - II) by the investigator.
 16. All previous IEC 's decisions (e.g., those leading to a negative decision or modified protocol) by other ECS or regulatory authorities for the proposed study (whether in the same location or elsewhere) and an indication of modification(s) to the protocol made on that account. The reasons for previous negative decisions must be provided.
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Appendix - II

Undertaking by the Investigator

1. Full name, address and title of the Investigator
2. Name and address of the medical college, hospital or other facility where the clinical trial will be conducted: Education, training & experience that qualify the Investigator for the clinical trial (Attach details including Medical Council registration number, and / or any other statement(s) of qualification(s))
3. Name and address of all clinical laboratory facilities to be used in the study.
4. Name and address of the Ethics Committee that is responsible for approval and continuing review of the study.
5. Names of the other members of the research team (Co- or sub-Investigators) who will be assisting the Investigator in the conduct of the investigation (s).
6. Protocol Title and Study number (if any) of the clinical trial to be conducted by the Investigator.
7. Committees: I have reviewed the clinical protocol thoroughly and agree that it contains all the necessary information to conduct the study. I will not begin the study until all necessary Ethics Committee and regulatory approvals have been obtained.

I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the Sponsor and prior review and documented approval / favorable opinion from the Ethics Committee of the amendment, except where necessary to eliminate an immediate hazard(s) to the trial Subjects or when the change(s) involved are only logistical or administrative in nature.

I agree to personally conduct and/or supervise the clinical trial at my site.

I agree to inform all Subjects, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent and ethics committee review and approval specified in the GCP guidelines are met.

I agree to report to the Sponsor all adverse experiences that occur in the course of the investigation(s) in accordance with the regulatory and GCP guidelines.

I have read and understood the information in the Investigators brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues and, employees assisting in the conduct of the study are suitably qualified and experienced and they have been informed about their obligations in meeting the commitments in the trial.

I agree to maintain adequate and accurate records and to make those records available for audit / inspection by the Sponsor, Ethics Committee, Licensing Authority or their authorized representatives, in accordance with regulatory and GCP provisions. I will fully cooperate with any study related audit conducted by regulatory officials or authorized representatives of the Sponsor.

I agree to promptly report to the Ethics Committee all changes in the clinical trial activities and all unanticipated problems involving risks to human Subjects or others.

I will maintain confidentiality of the identification of all participating study patients and assure security and confidentiality of study data.

I agree to comply with all other requirements regarding the obligations of clinical Investigators and all other pertinent requirements in a GCP and all applicable regulatory requirements.

8. Signature of Investigator with Date

Appendix - III

Contents of the Proposed Protocol for Conducting Clinical Trials in India

i. Title Page

- a. Full title of the clinical study,
- b. Protocol number, along with protocol version number,
- c. Complete name and address of the Sponsor

List of the Investigators who are conducting the study, their respective institutional affiliations and site locations, as well as the name(s) of clinical laboratories and other departments and/or facilities participating in the study. The IND name/number of the investigational drug.

ii. Table of Contents

A complete Table of Contents including a list of all Appendices.

1. Background and Introduction

- Preclinical experience
- Clinical experience

Previous clinical work with the new drug should be reviewed here and a description of how the current protocol extends existing data should be provided. If this is an entirely new indication, how this drug was considered for this should be discussed. Relevant information regarding pharmacological, toxicological and other biological properties of the drug/biologic/medical device, and previous efficacy and safety experience should be described.

2. Study Rationale

This section should describe a brief summary of the background information relevant to the study design and protocol methodology. The reasons for performing this study in the particular population included by the protocol should be provided.

3. Study Objective(s) (primary as well as secondary) and their logical relation to the study design.

4. Study Design

- Overview of the Study Design: Including a description of the type of study (i.e., double-blind, multicentre, placebo controlled, etc.), a detail of the specific treatment groups and number of study Subjects in each group and investigative site/Subject number assignment, and the type, sequence and duration of study periods.
- A brief description of the methods and procedures to be used during the study.
- Discussion of Study Design: This discussion details the rationale for the design chosen for this study.
- Inclusion Criteria
- Exclusion Criteria

7. Study Assessments - plan, procedures and methods to be described in detail

8. Study Conduct stating the types of study activities that would be included in this section would be: medical history, type of physical examination, blood or urine testing, electrocardiogram (ECG), diagnostic testing such as pulmonary function tests, symptom measurement, dispensation and retrieval of medication. Subject cohort assignment, adverse event review, etc.

Each visit should be described separately as Visit 1, Visit 2, etc.

Discontinued Subjects: Describes the circumstances for Subject withdrawal, dropouts, or other reasons for discontinuation of Subjects. State how drop outs would be managed and if they would be replaced. Describe the method of handling of protocol waivers, if any. The person(s) who approves all such waivers should be identified and the criteria used for specific waivers should be provided.

Describes how protocol violations will be treated, including conditions where the study will be terminated for non-compliance with the protocol.

9. Study Treatment

- Dosing schedule (dose, frequency, and duration of the experimental treatment) Describe the administration of placebos and/or dummy medications if they are part of the treatment plan. If applicable, concomitant drug(s), their doses, frequency, and duration of concomitant treatment should be stated.
- Study drug supplies and administration: A statement about who is going to provide the study medication and that the investigational drug formulation has been manufactured following all regulations. Details of the product stability/ storage requirements and dispensing requirements should be provided.
- Dose modification for study drug toxicity: Rules for changing the dose or stopping the study drug should be provided.
- Possible drug interactions
- Concomitant therapy: The drugs that are permitted during the study and the conditions under which they may be used are detailed here. Describe the drugs that a Subject is not allowed to use during parts of or the entire study. If any washout periods for prohibited medications are needed prior to enrollment, these should be described here.
- Discontinuation from study treatment: The specific reasons from early discontinuation from the study (viz. discontinuation due to treatment failure (with a description of what would constitute treatment failure) or discontinuation due to other causes (e.g., adverse events, withdrawal of consent, etc.).
- Blinding procedures: A detailed description of the blinding procedure if the study employs a blind on the Investigator and/or the Subject
- Unblinding procedures: If the study is blinded, the circumstances in which unblinding may be done and the mechanism to be used for unblinding should be given

10. Adverse Events: Description of expected adverse events should be given. Procedures used to evaluate an adverse event should be described.

11. Ethical Considerations: Give the summary of:

- Risk/benefit assessment;
- Ethics Committee review and communications.
- Informed consent process
- Statement of Subject confidentiality including ownership of data and coding procedures

12. Study Monitoring and Supervision: A description of study monitoring policies and procedures should be provided along with the proposed frequency of site monitoring visits, and who is expected to perform monitoring.

Case Record Form (CRF) completion requirements, including who gets which copies of the forms and any specifics required in filling out the forms CRF correction requirements, including who is authorized to make corrections on the CRF and how queries about study data are handled and how errors, if any, are to be corrected should be stated, investigator study files, including what needs to be stored following study completion should be described.

13. Investigational Product Management

- Give Investigational product description and packaging (stating all ingredients and the formulation of the investigational drug and any placebos used in the study)
- The precise dosing required during the study
- Method of packaging, labeling, and blinding of study substances
- Method of assigning treatments to Subjects and the Subject identification code numbering system
- Storage conditions for study substances
- Investigational product accountability: Describe instructions for the receipt, storage, dispensation, and return of the investigational products to ensure a complete accounting of all Investigational products received, dispensed, and returned/destroyed.
- Describe policy and procedure for handling unused investigational products.

14. Data Analysis:

Provide details of the statistical approach to be followed including sample size, how the sample size was determined, including assumptions made in making this determination, efficacy endpoints (primary as well as secondary) and safety endpoints.

Statistical analysis: Give complete details of how the results will be analyzed and reported along with the description of statistical tests to be used to analyze the primary and secondary endpoints defined above. Describe the level of significance, statistical tests to be used, and the methods used for missing data; method of evaluation of the data for treatment failures, non-compliance, and Subject withdrawals; rationale and conditions for any interim analysis if planned. Describe statistical considerations for Pharmacokinetic (PK) analysis, if applicable.

15. Undertaking by the Investigator

16. Appendices:

1. provide a study synopsis,
 2. copies of the informed consent documents (patient information sheet, informed consent form etc.);
 3. CRF and other data collection forms;
 4. a summary of relevant pre-clinical safety information and any other documents referenced in the clinical protocol."
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